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I also certify that by virtue of an assignment registered under the Patents Act 1977, the application is now proceeding in the name as substituted

.

I also certify that the attached copy of the request for grant of a Patent (Form 1/77) bears an amendment, effected by this office, following a request by the applicant and agreed to by the Comptroller-General

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

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Signed Andrew Gersey

Dated 20 August 2003

GB0227345.6

By virtue of a direction given under Section 30 of the Patents Act 1977, the application is proceeding in the name of

OPTINOSE AS,
Lokkaskogen 18c,
0773 Oslo,
Norway

Incorporated in Norway,

[ADP No. 08042905001]

Patents Form 1/77

Patents Act 1977
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THE PATENT OFFICE
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02 E765737-9 D01631
P01/7700 0.00-0227345.6

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form.)

The Patent Office

Cardiff Road
Newport
Gwent NP9 1RH

Fee: £0

1. Your reference

44854.GB02/SJNG

2. Patent application number
(The Patent Office will fill in this part)

22 NOV 2002 0227345.6

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

Team Holdings (UK) Ltd
Cokenach, Barkway
Hertfordshire
SG8 8DL
United Kingdom

14/11/03

Patents ADP number *(if you know it)* 08033557001

SECTION 8(3)(7) ACT/APPLICATION FILED

If the applicant is a corporate body, give the country/state of incorporation

GB

4. Title of the invention

Dispenser and Dispensing Method

5. Full name, address and postcode in the United Kingdom to which all correspondence relating to this form and translation should be sent

~~Reddie & Grose~~
~~16 Theobalds Road~~
~~LONDON~~
~~WC1X 8PL~~

FRY HEATH & SPENCE
THE GABLES
MASSETTS RD
HORLEY SURREY
RH6 7DQ

91001

DLS 9554001

Patents ADP number *(if you know it)*

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application *(If you know it)*	Date of filing *(day/month/year)*
GB	0215904.4	09/07/02
		09 July 2002

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day/month/year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d))

YES

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document.

Continuation sheets of this form	
Description	8
Claim(s)	3
Abstract	
Drawing(s)	7 + 7

10. If you are also filing any of the following, state how many against each item.

Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	1
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Signature: Reddie & Grose — Date: 21 November 2002

12. Name and daytime telephone number of person to contact in the United Kingdom: S J N GOODMAN 01223 360350

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Notes

a) *If you need help to fill in this form or you have any questions, please contact the Patent Office on 0645 500505.*

b) *Write your answers in capital letters using black ink or you may type them.*

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Dispenser and Dispensing Method

The invention relates to a dispenser and a dispensing method, in particular for drug-delivery applications.

Nasal delivery for a range of powder and liquid drugs has been established for some time and there is a range of existing products on the market which uses this method. The oral route for drug delivery is still far more prevalent but there is an increasing amount of research being carried out in the area of nasal delivery technologies.

"Form fill and seal" packaging using vacuum forming and laminating technologies, typically using aluminium foil or polymer materials, is well established for a range of product types. This includes products in the pharmaceutical sector (including capsule blister packs and sachets for lyophilised drugs) and for a large range of other types of product (e.g. coffee sachets and adhesives). It is also known in many applications, and especially in non-pharmaceutical applications, to make "form, fill and seal" plastic products incorporating welded-in injection-moulded spouts and caps.

In the pharmaceutical field, US patent no. 5215221 describes a disposable unit-dose dispenser for a powdered medicament, which comprises a domed gas chamber separated from a dose chamber by a frangible seal. When pressure is applied to the chamber by squeezing, the gas pressure within the chamber rises and this pressure ruptures the seal. The pressurised gas then suddenly exits through the dose chamber, where the powdered medicament is fluidised and dispensed through a delivery tube, carried by the gas flow.

This prior art dispenser suffers a significant disadvantage in that it is very difficult to fabricate the frangible seal such that it will reliably rupture at a predetermined gas pressure, as required to fluidise and dispense the medicament accurately.

The invention provides a dispenser and a dispensing method as defined in the appended independent claims, to which reference should now be made. Preferred or advantageous features of the invention are defined in dependent subclaims.

The invention may thus advantageously provide a dispenser in which, as a gas-filled chamber or pouch is squeezed by a user, a seal between the chamber and a nozzle is ruptured or opened mechanically by an opening means, or opening mechanism, and not only by the elevated gas pressure within the chamber. The seal may thus be ruptured when the chamber has been deformed to a predetermined shape, or position, at which the opening means ruptures the seal. The structure of the chamber may advantageously be designed to deform in a predetermined manner, so that its volume (and therefore the gas pressure within it) is always the same when the seal is ruptured, in order to deliver a dispensate, such as a powder or a liquid, out of the nozzle in a predictable manner.

The invention may therefore provide a significant improvement over the dispenser of US 5215221 described above, particularly in critical applications such as drug delivery where the delivered jet or cloud of liquid or powder needs to be tightly controlled; in such applications it is essential that the seal fails in a repeatable and reproducible manner. It must not be the case that its failure point may be influenced by, say, the

rate of application of pressure, nor must it be possible to reduce the load at which the seal fails by fatigue, e.g. through cyclic loading of the gas chamber below its critical pressure limit. Also, the failure of the seal should not depend on, for example, ambient conditions such as temperature or humidity, or previous storage conditions. Similarly, the pressure profile and gas flow during and following the failure of the seal needs to be as uniform, or predictable, as possible.

In a preferred embodiment, a dispenser according to the invention comprises a chamber in the form of a pouch, optionally of the "form, fill and seal" type, and a nozzle, which may be injection-moulded, as the basis of a single-use disposable dispenser product that will allow the generation and delivery of a cloud of powder particles or liquid droplets. In the dispenser the gas-filled pouch is separated from the nozzle by a seal, which may be a separate component. The nozzle may incorporate a dispensate chamber. Once the seal is broken, the raised pressure in the pouch will cause the gas and hence the dispensate in the dispensate chamber to be expelled through the nozzle.

However, the seal will not fail solely under the effects of pressure generated by squeezing the pouch. It will be controlled by other features or characteristics. The separation of the rupturing of the seal from the application of pressure is key to the invention. It gives the ability to "tune" a predetermined pressure at which the barrier seal is broken and to prevent premature or undesired failure of the seal due to misuse or abuse (including adverse storage conditions) of the device. It also allows increased control of the flow of pressurised

gas, and hence the characteristics of the flow of powder or liquid, out of the nozzle.

In an alternative embodiment, the dispensate may be stored within the chamber or pouch, or within the nozzle upstream of the seal, before dispensing.

The invention may thus enable the manufacture of a low-cost disposable dispenser, such as a drug delivery device, based on manufacturing processes that are separately already well-established. It may also allow extremely tight controls on the delivery characteristics of such a low-cost device.

Specific Embodiments and Best Mode of the Invention

Specific embodiments of the invention will now be described by way of example, with reference to the accompanying drawings, in which:

Figure 1 is a perspective view of a first dispenser embodying the invention, before use;
Figure 2 is a perspective view of the dispenser of figure 1 after use;
Figure 3 is a longitudional section of the dispenser of figure 1;
Figure 4 is a longitudional section of the dispenser of figure 2;
Figure 5 is a perspective view of a second dispenser embodying the invention, before use;
Figure 6 is a perspective view of the dispenser of figure 5 after use;
Figure 7 is a longitudinal section of the dispenser of figure 5 illustrating a first opening mechanism, before use;

Figure 8 is a longitudinal section of the dispenser of figure 7 after use;

Figure 9 is a longitudinal section of the dispenser of figure 5 embodying a second opening mechanism, before use;

Figure 10 is a longitudinal section of the dispenser of figure 9 after use;

Figure 11 is a longitudinal section of the dispenser of figure 5 showing a third opening mechanism, before use;

Figure 12 is a longitudinal section of the dispenser of figure 11 after use;

Figure 13 is a longitudinal section of the dispenser of Figure 5 illustrating a fourth opening mechanism, before use;

Figure 14 is a longitudinal section of the dispenser of figure 13 after use;

Figure 15 is a longitudinal section of the dispenser of figure 5 illustrating a fifth opening mechanism, before use; and

Figure 16 is a longitudinal section of the dispenser of figure 15 after use.

Figure 1 illustrates a single-shot disposable nasal insuflator drug delivery device comprising an essentially hemispherical, or dome-shaped, pouch 2 containing gas separated by a seal 4 from a nozzle 6 comprising a drug chamber. A sharp spike extends from an inside surface of the pouch, at the centre of the dome opposite the seal. When a force is applied to the dome it collapses in a controlled manner such that when the dome is significantly collapsed, the spike contacts the barrier seal. As a result of this contact, and in conjunction with the applied gas pressure, the barrier seal ruptures and the pressurised gas flows rapidly out of the nozzle, taking with it the powdered drug, which is of particle size

profile appropriate to give the necessary fine particle fraction.

As the pouch is compressed, the pressure in the gas rises but this is not in itself sufficient to cause rupture of the seal. It is only when the puncturing spike formed in the base of the hemispherical pouch contacts and bursts the seal that the gas can exit. The geometry (e.g. curvature, wall section) of the pouch is designed such as to give very repeatable deformation, such that the pressure in the gas at the point when the spike ruptures the seal will also be extremely repeatable.

Figures 5 and 6 illustrate a dispenser fabricated using a "form, fill and seal" approach, using a combination of vacuum-forming techniques with aluminium foil or metallised polymer materials. The dispenser also incorporates an injection-moulded nozzle but is of a different layout from the embodiment of figures 1 to 4 in that the pouch, or gas chamber, 2 is squeezed by applying a force perpendicular to the axis of the nozzle rather than parallel to it. Experience shows that this is a beneficial orientation for nasal drug delivery devices, but different orientations may be appropriate for other applications. (In figures 5 and 6, and in figures 7 to 16, the same reference numerals as in figures 1 and 2 have been used where appropriate).

Figures 7 to 16 illustrate various mechanisms for rupturing a seal 4 between a gas chamber 2 and a nozzle 6, in order to entrain a drug or other substance 10 for delivery.

In figure 7, when the pouch is squeezed, a hinged lever mechanism within the pouch causes a sharp point to contact

a membrane seal between the pouch and a drug chamber at the base of the nozzle. When the pouch is squeezed to a certain point, the sharp point causes the membrane seal to rupture, aided by the gas pressure, as shown in figure 8.

The embodiment of figure 9 is similar in principle to that of figures 7 and 8, but employs a different lever arrangement to bring the point into contact with an edge of the membrane seal.

In figure 11, the seal comprises a piston, or plug, 12 which fits within a bore 14 at the base of the nozzle. The plug may also have a seal component mounted on it, such as a rubber grommet or the like. When the pouch is compressed, a lever mechanism coupled to the plug causes the plug to begin retracting from the nozzle bore. When the pouch is squeezed to a specific point, the plug is fully withdrawn from the bore allowing the pressurised gas to exit as required, as shown in figure 12.

In figure 13, the seal again comprises a plug 12 which fits within a bore 14. As the pouch is compressed it initially has no contact with the internal mechanism. However, towards the end of the compression, as the pressure approaches its predetermined critical limit, the mechanism is acted upon and begins to push the plug forwards inside the nozzle. At a predetermined critical point, the plug is pushed out of the bore into a widened section of the nozzle, thus allowing the pressurised gas to exit as required. Figure 14 shows the dispenser after use.

Figure 15 illustrates a seal comprising a hinged flap 16 which seats on a seat 18 at the base of the nozzle. The flap may be biassed into its seated position or may be

adhered to the seat. When the pouch is compressed, it initially has no contact with the internal mechanism. However, towards the end of the compression, as the pressure approaches its critical predetermined limit, the mechanism is acted upon and begins to apply a torque to the flap. At the critical predetermined point, the flap is pulled away from the sealing face of the nozzle, rupturing the seal and allowing the pressurised gas to exit as required. Figure 16 illustrates the mechanism after use.

In the various implementations of this invention, opening mechanism geometries, barrier seal burst pressures, and different nozzle types and geometries, may be designed to produce dispensers with a range of applications. For example in the field of drug delivery devices, the design may be varied to produce dispensers for targeting different zones of the nasal cavity.

It may also be possible to implement the invention in a multi-shot device with one or more sacrificial elements that are replaced for each operation in conjunction with other components that are reused each time.

The invention may also find application in a range of non-healthcare applications where a one-off controlled release of a powder or liquid is required.

Claims

1. A dispenser comprising;

a gas-filled chamber of variable volume;

a nozzle coupled to the chamber and from which a dispensate is deliverable, carried by the gas from the chamber;

a seal between the chamber and the nozzle; and

a means for opening the seal on reduction of the chamber volume to a predetermined volume, to allow the gas pressurised by the reduction in chamber volume to flow through the nozzle.

2. A dispenser according to claim 1, in which the chamber is deformable to reduce its volume.

3. A dispenser according to claim 1 or 2, in which the dispensate is housed in the nozzle prior to delivery.

4. A dispenser according to any preceding claim, in which the seal comprises a membrane separating the chamber from the nozzle and the opening means comprises a rupturing element for rupturing the membrane.

5. A dispenser according to claim 4, in which the rupturing means extends from an inner surface of the chamber and, as the volume of the chamber is reduced, the rupturing means penetrates and ruptures the membrane.

6. A dispenser according to claim 4, in which the opening means further comprises a lever coupled to the

rupturing element, for driving the rupturing element to rupture the membrane as the volume of the chamber is reduced.

7. A dispenser according to claim 4,5 or 6, in which the rupturing means ruptures an edge of the membrane.

8. A dispenser according to claim 1, 2 or 3, in which the seal comprises a piston slidably receivable within a bore.

9. A dispenser according to claim 8, in which the opening means drives the piston out of the bore as the volume of the chamber is reduced.

10. A dispenser according to claim 8 or 9, in which the opening means further comprises a lever coupled to the piston.

11. A dispenser according to claim 1, 2 or 3, in which the seal comprises a hinged flap, which seals against a seat, and the opening means acts to lift the flap away from the seat.

12. A dispenser according to claim 11, in which the opening means comprises a lever coupled to the flap, for lifting the flap away from the seat as the volume of the chamber is reduced.

13. A dispensing method for delivering a dispensate, comprising the steps of;

reducing the volume of a gas-filled chamber to increase the pressure of the gas;

when the chamber volume is reduced to a predetermined volume, operating an opening means to open a seal between the chamber and a nozzle, so allowing the pressurised gas to escape from the chamber and flow through the nozzle; and

delivering the dispensate from the nozzle in the gas flow.

14. A method according to claim 13, in which the seal comprises a membrane and the opening means operates to rupture the membrane.

15. A method according to claim 13, in which the seal comprises a piston slidably receivable within a bore and the opening means operates to slide the piston out of the bore.

16. A method according to claim 13, in which the seal comprises a hinged flap which seals against a seat, and the opening means operates to hinge the flap away from the seat.

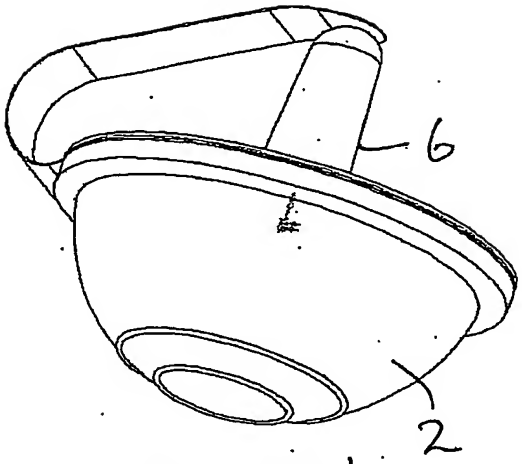

FIGURE 1

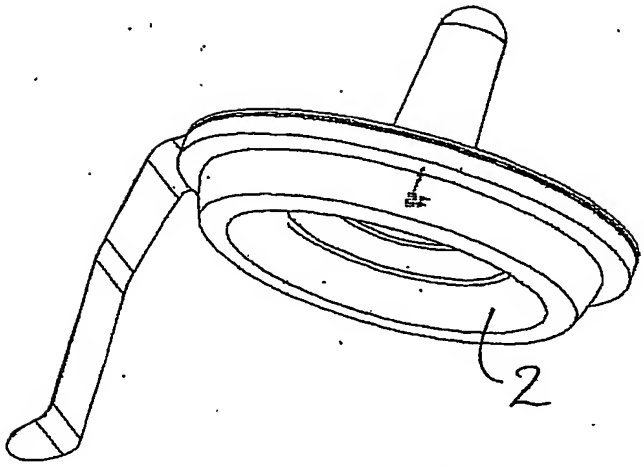

FIGURE 2

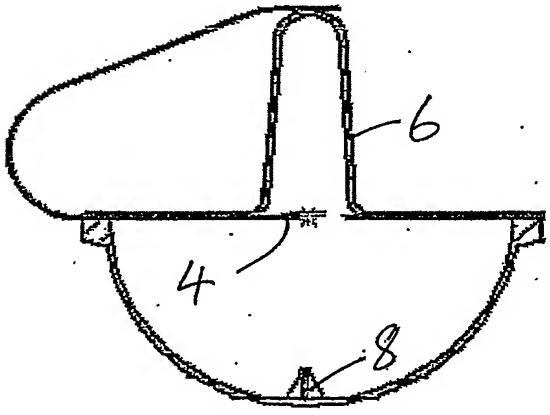

FIGURE 3

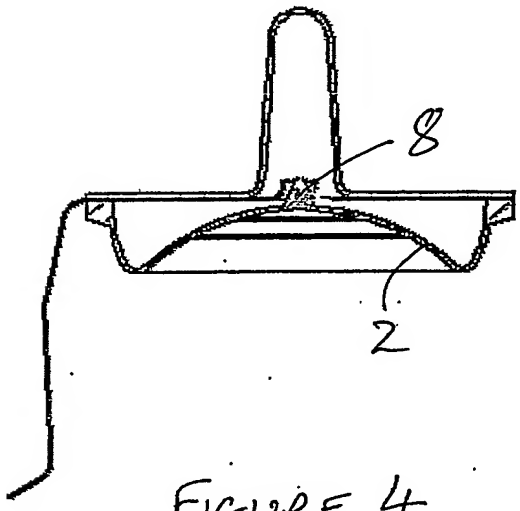

FIGURE 4

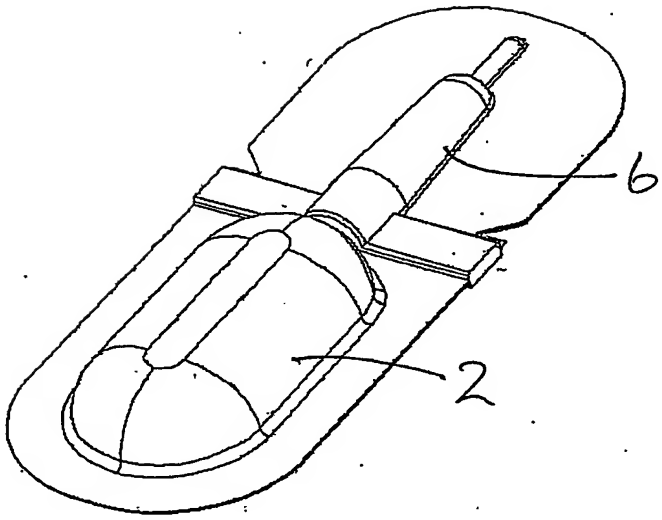

FIGURE 5

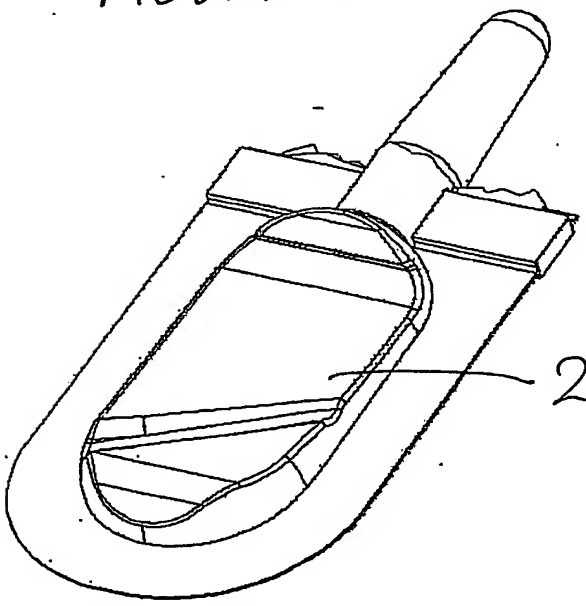

FIGURE 6

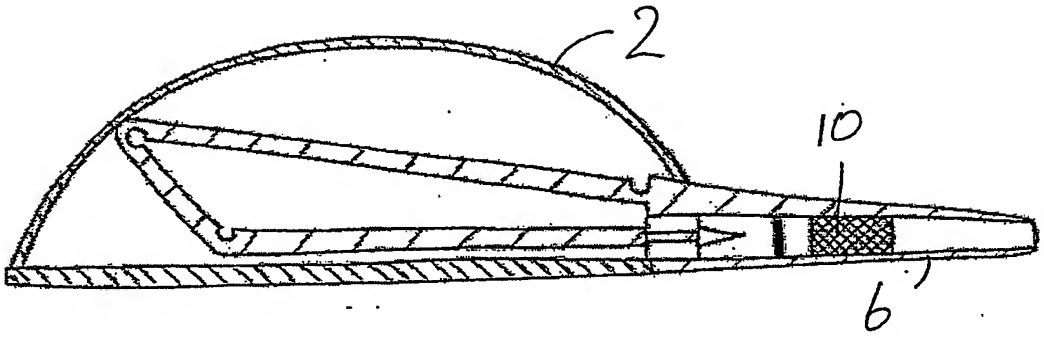

FIGURE 7

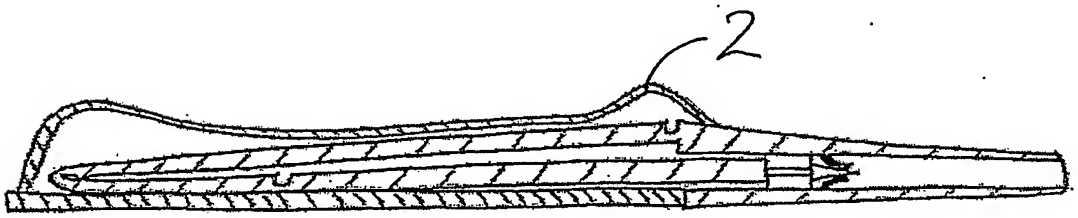

FIGURE 8

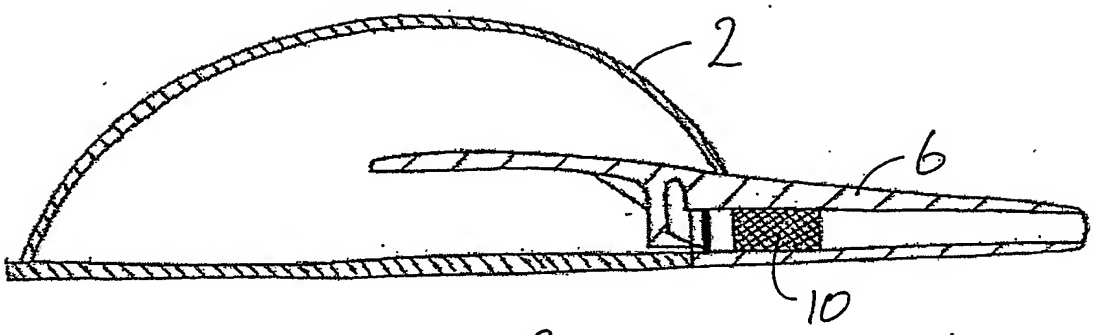

FIGURE 9

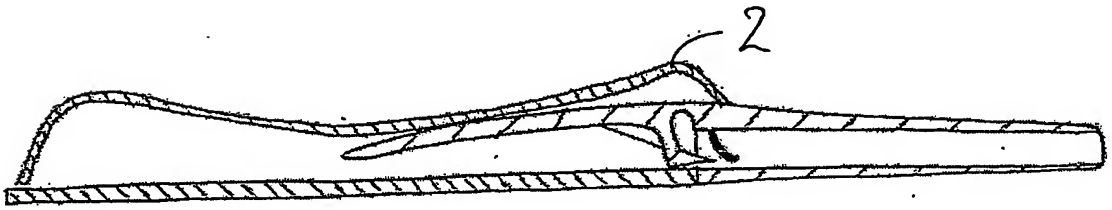

FIGURE 10

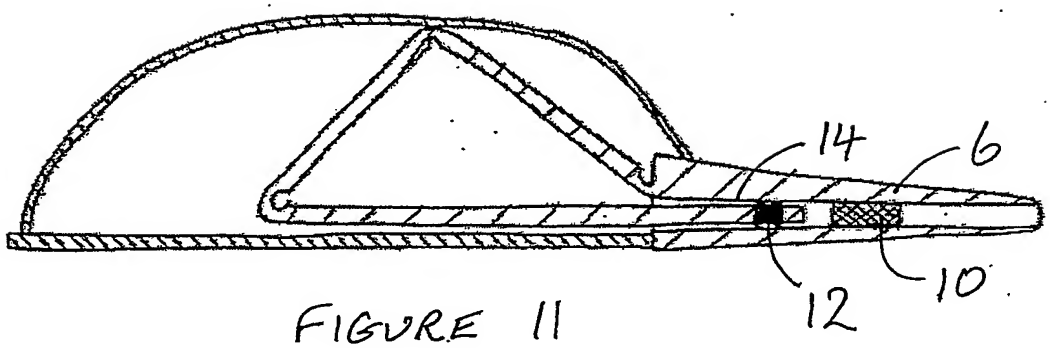

FIGURE 11

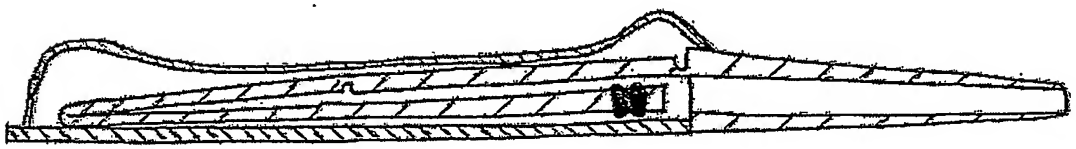

FIGURE 12

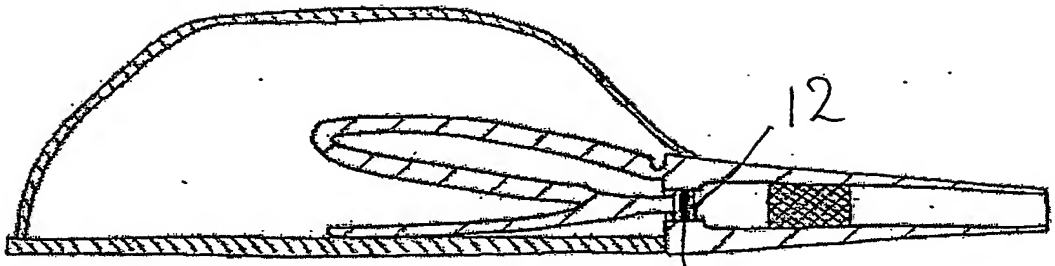

FIGURE 13

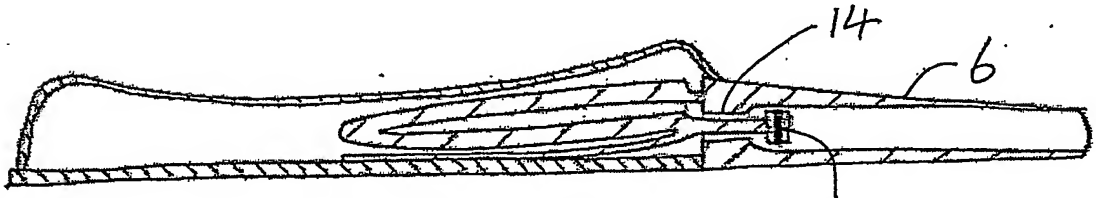

FIGURE 14

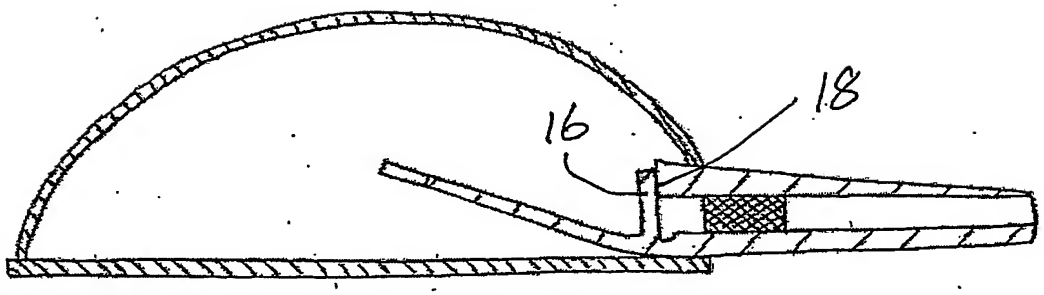

FIGURE 15

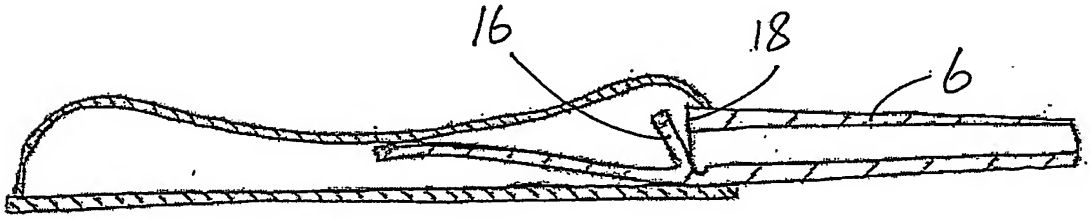

FIGURE 16.